

## Outcomes of Chronic Dialysis Patients Admitted to the Intensive Care Unit

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### ABSTRACT

Admission rates and outcomes of patients who have ESRD and are admitted to an intensive care unit (ICU) are not well defined. We conducted a historical cohort study using a prospective regional ICU database that captured all 11 adult ICUs in Winnipeg, Canada. Between 2000 and 2006, there were 34,965 total admissions to the ICU, 1173 (3.4%) of which were patients with ESRD. The main admission diagnoses among patients with ESRD were cardiac disease (31%), sepsis (15%), and arrest (10%). Compared with other patients in the ICU, those with ESRD were significantly younger but had more diabetes, peripheral arterial disease, and higher APACHE II (Acute Physiology and Chronic Health Evaluation II) scores; mean length of stay in the ICU was similar, however, between these two groups. Restricting the analysis to first admissions to the ICU, unadjusted in-hospital mortality was higher for patients with ESRD (16 versus 11%;  $P < 0.0001$ ), but this difference did not persist after adjustment for baseline illness severity. In conclusion, although ESRD associates with increased mortality among patients who are admitted to the ICU, this effect is mostly a result of comorbidity.

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The prevalence of ESRD continues to grow steadily and now exceeds 1.5 cases per 1000 population in the United States.<sup>1</sup> Although admissions for infection and cardiovascular disease are common in patients with ESRD, little is known about the rate or length of stay (LOS) of ICU admissions.<sup>2</sup> Similarly, the outcomes of patients who have ESRD and are admitted to the ICU are not well described. Until recently, it was assumed that patients with ESRD had outcomes similar to patients with acute kidney injury (AKI); however, data from a large UK database suggested ICU mortality is intermediate between patients without ESRD and those with oliguric AKI.<sup>3</sup> Interestingly, much of the increased mortality risk in patients with ESRD was attributable to comorbidities and illness severity. The same study estimated that the ESRD-specific ICU admission rate was 6 per 100 patients with ESRD per year.

It is difficult to extrapolate these results to the North American setting because substantial demographic, case-mix, practice pattern, morbidity, and

mortality differences may exist between North American and European ESRD populations.<sup>4–6</sup> Unfortunately, corresponding data on patients who have ESRD and are admitted to the ICU in North American centers are sparse,<sup>7–9</sup> and *in toto* these studies report on only 239 patients with ESRD. Only one study<sup>7</sup> compared in-hospital mortality in patients with ESRD ( $n = 57$ ), patients without ESRD ( $n = 1219$ ), and patients with AKI ( $n = 254$ ), reporting rates of 14, 9, and 34%, respectively. A more robust estimation of the mortality of patients who have ESRD and are admitted to the ICU in

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North America is needed to guide clinicians in estimating prognosis and to avoid inappropriate withholding of ICU care on the basis of ESRD status alone.

The objectives of our study were to estimate the rate of ESRD admissions to ICU in a regional North American center, to examine the outcomes of these patients after admission, and to estimate the excess mortality risk attributable to ESRD status *per se*. We hypothesized that the excess ICU mortality risk associated with long-term dialysis status would be modest and less than that associated with AKI that requires dialysis.

## RESULTS

During the study period, there were 34,965 total admissions to ICU, 1173 (3.35%) of which included patients with ESRD. The most common admitting diagnoses for patients with ESRD were cardiovascular (*e.g.*, congestive heart failure, myocardial infarction, arrhythmia) in 31%, sepsis in 15%, and cardiac arrest (mechanism not specified) in 10%.

As shown in Figure 1, crude admission rates were several-fold higher in the prevalent adult ESRD population than in the adult non-ESRD population in Manitoba (15.6 admissions per 100 prevalent patients with ESRD per year *versus* 0.58 per 100 prevalent patients without ESRD per year). Age and gender standardization attenuated the ESRD admission rate, suggesting that some of the difference was attributable to differences in age and gender distribution between the adult ESRD and general populations.

The mean length of stay (LOS) for patients with ESRD during the same period was 4.3 d. Using these figures, mean ICU use by dialysis patients during the study period, calculated as

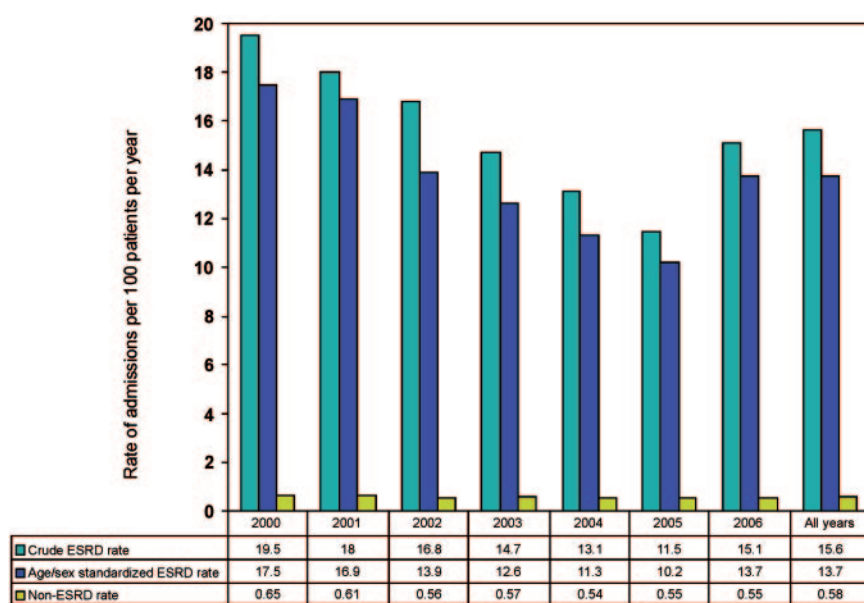
mean admission rate multiplied by mean LOS, was 67 ICU bed-days per 100 dialysis patients per year.

Of the total admissions during the study period, 28,114 (80.4%) were first admissions and 6851 (19.6%) were repeat admissions. To avoid potential distortions as a result of the nonindependence of repeated admissions, we restricted the analysis to first admissions. Of the first admissions, 619 had ESRD. Among the patients without ESRD, 935 (3.32%) developed AKI defined as requirement for dialysis or continuous renal replacement therapy (see the Concise Methods section).

Table 1 illustrates demographic, case-mix, and outcome differences between patients with and without ESRD. Patients with ESRD were younger and had higher rates of diabetes and vascular disease than patients without ESRD. A higher proportion of the group with ESRD had cardiac arrest, sepsis, or multiorgan failure. Several physiologic variables were statistically significantly different between the groups. Acute Physiology and Chronic Health Evaluation II (APACHE II) scores were higher in patients with than without ESRD, as expected, an effect that persisted even after subtracting the renal component of the score (renally adjusted APACHE II; see the Concise Methods section). LOS was similar, as was the Therapeutic Intervention Scoring System (TISS) score, which is an accepted measure of ICU resource use.<sup>10</sup> Readmissions to ICU within 3 d and readmissions during same hospital stay were roughly twice as frequent in the group with ESRD. Unadjusted in-hospital mortality among patients with ESRD was significantly higher than in patients without ESRD.

Table 2 highlights differences between patients with and without ESRD and with AKI requiring dialysis. The patients with AKI were generally the sickest, followed by patients with ESRD, as suggested by the higher proportion of patients in these groups who had cardiac arrest, sepsis, multiorgan failure, or more severe physiologic or biochemical derangements. APACHE II scores were highest for patients with AKI, as expected, followed by patients with ESRD. Interestingly, this relationship was still evident in the renally adjusted score. LOS and TISS score were similar in ESRD and the non-AKI groups but were significantly higher in the patients with AKI. Readmissions to ICU were roughly twice as frequent in the ESRD and AKI groups. Unadjusted in-hospital mortality among patients with ESRD was almost twice that in control subjects but less than half that in patients with AKI.

Using logistic regression, we adjusted the odds ratio (OR) associated with ESRD status for the effects of potential confounders. After adjustment, the OR associated with ESRD status was close to unity and not statistically significant (Table 3). When a reduced model was derived using backward stepping (Table 4), ESRD status was not statistically significant and was excluded from



**Figure 1.** The graph shows rates of admission to the ICU among patients with ESRD versus the general population.

**Table 1.** Comparison of admission characteristics and raw outcomes in patients with and without ESRD

Characteristic	Without ESRD (n = 27,495)	With ESRD (n = 619)	P <sup>a</sup>
Age (yr)	64	62	0.0002
Male gender (%)	61.2	54.4	0.0006
Diabetes (%)	21.7	52.3	<0.0001
CAD (%)	14.3	15.7	0.3
Stroke (%)	7.2	10.3	0.0027
Peripheral arterial disease (%)	12.3	29.7	<0.0001
Cancer (%)	13.1	10.5	0.06
Sepsis (%)	6.5	15.8	<0.0001
Mechanical ventilation (%)	41.7	42.0	0.9
Surgical status (%)			<0.0001
elective	19.0	7.4	
emergent	8.7	8.9	
nonsurgical	72.2	83.7	
Organ failure (%)			0.007
0	43.3	43.1	
1	41.7	38.1	
2	11.8	13.1	
≥3	3.2	5.7	
Temperature (°C)	36.8	36.7	0.1
MAP (mmHg)	79	77	0.06
Heart rate (/min)	85	87	0.02
Respiratory rate (/min)	20	22	0.0002
PaO <sub>2</sub> (FiO <sub>2</sub> <0.5)	109	115	0.08
Serum sodium (mmol/L)	139	138	0.0001
Serum potassium (mmol/L)	4.0	4.7	0.0001
Serum creatinine (μmol/L)	112	577	0.0001
Hematocrit (%)	33	29	0.0001
WBC count (×10 <sup>3</sup> )	13	14	0.002
GCS score	14	13	0.01
APACHE II	15	24	0.0001
Renally adjusted APACHE II <sup>b</sup>	14	20	0.0001
TISS score	23	23	0.7
ICU LOS (days)	4.2	4.3	0.9
In-hospital mortality (%)	10.7	15.5	<0.0001
Readmission within 3 d (%)	2.2	4.4	0.0002
Readmission during hospital stay (%)	4.9	12.0	<0.0001

CAD, coronary artery disease; GCS, Glasgow Coma Scale; WBC, white blood cell.

<sup>a</sup>T test for Gaussian distributions, Mann-Whitney U test for non-Gaussian distributions,  $\chi^2$  test for dichotomous variables.

<sup>b</sup>See text. Calculated by subtracting renal component from APACHE II score.

the final model. In a sensitivity analysis using last admissions instead of first admissions, the adjusted OR for death associated with ESRD was slightly higher but not statistically different from unity (1.17; 95% confidence interval 0.93 to 1.45).

## DISCUSSION

The main findings of our analysis were that (1) patients with ESRD were admitted to the ICU much more frequently than

that observed for the general population; (2) patients with ESRD experienced less than half the crude mortality of patients with AKI in the ICU; and (3) ESRD status, although identifying a discrete group with worse ICU prognosis, was not associated with higher in-hospital mortality after multivariate adjustment, suggesting that the higher mortality was driven by comorbid conditions and illness severity rather than ESRD status *per se*.

Our results are congruent with those of a large UK study. Hutchison *et al.*<sup>3</sup> examined admission rates and outcomes of patients who had ESRD and were admitted to ICUs in the United Kingdom using the Intensive Care National Audit and Research Centre database. ICU admission and bed use rates for patients with ESRD were six admissions and 32 ICU bed-days per 100 patients with ESRD per year, respectively, higher than for the nondialysis UK population but approximately half that observed in our study. In-hospital mortality and APACHE scores for patients with ESRD were similar to those in our study, but their group without ESRD had higher mortality than ours. Within the control group of the Hutchison study, patients who had oliguric AKI were noted to have a mortality of 70.3%. Differences in case mix between UK and Canadian dialysis patients and differences in ICU practice patterns and referral filter biases between the United Kingdom and Canada could account for some of these outcome differences.

Several smaller, single-center studies also support our findings. A study by Clermont *et al.*<sup>7</sup> reviewed 1530 admissions to eight ICUs during a 10-mo period in Pittsburgh, Pennsylvania. Only 57 of the admitted patients had ESRD, 254 developed AKI on the basis of acute changes in serum creatinine, and 1219 had no renal failure. They found, as in our study, that patients with ESRD had intermediate acute illness severity scores and mortality. In-hospital mortality in their study was lower than in our study (34% in patients with AKI, 14% in patients with ESRD, and 9% in control subjects). Manhes *et al.*<sup>8</sup> studied at 92 long-term dialysis patients who were admitted to the ICU and found mortality rates in hospital of 38%, with mean ICU LOS 6.2 ± 9.9 d. Dara *et al.*<sup>9</sup> examined mortality of 93 patients who had ESRD and were admitted to the ICU and found ICU, hospital, and 30-d mortality rates to be 9, 16, and 22%, respectively.

The unadjusted in-hospital mortality of patients with ESRD in the three largest studies (ours, Hutchison *et al.*,<sup>3</sup> and Clermont *et al.*<sup>7</sup>) was less than half the mortality observed in patients with AKI. After adjustment for potential confounders, the impact of ESRD status on in-hospital mortality was modest in all three studies, conferring a <25% increase in risk. That the outcomes of patients with ESRD seem relatively consistent across multiple regions that have different case mixes and practice patterns for dialysis and ICU suggests these observations are robust. Clinically, because prognosis depends more on comorbid conditions than on ESRD status, it seems reasonable to base decisions about treatment and ICU admission on comorbid conditions, not on ESRD status.

There are several important limitations to this analysis. One of the most important is that ICU admission filter biases for

**Table 2.** Admission characteristics and raw outcomes in patients with and without ESRD and with and without AKI requiring dialysis

Variable	Overall (n = 28,114)	With ESRD (n = 619)	Without ESRD	
			With AKI (n = 935)	Without AKI (n = 26,560)
Age (yr)	64.0	61.6 <sup>a</sup>	63.3 <sup>b</sup>	63.8 <sup>b</sup>
Male gender	61.1	54.4 <sup>a</sup>	57.1 <sup>a</sup>	61.4 <sup>b</sup>
Diabetes	22.4	52.3 <sup>a</sup>	37.5 <sup>b</sup>	21.1 <sup>c</sup>
CAD	14.3	15.7 <sup>a</sup>	12.0 <sup>b</sup>	14.4 <sup>a</sup>
Stroke	7.2	10.3 <sup>a</sup>	6.7 <sup>b</sup>	7.2 <sup>b</sup>
Peripheral arterial disease	12.7	29.7 <sup>a</sup>	16.6 <sup>b</sup>	12.2 <sup>c</sup>
Cancer (%)	13.1	10.5 <sup>a</sup>	14.2 <sup>b</sup>	13.1 <sup>a,b</sup>
Arrest	5.8	10.2 <sup>a</sup>	8.4 <sup>a</sup>	5.6 <sup>b</sup>
Sepsis	6.7	15.8 <sup>a</sup>	36.6 <sup>b</sup>	5.5 <sup>c</sup>
Mechanical ventilation	41.7	42.0 <sup>a</sup>	66.0 <sup>b</sup>	41.0 <sup>a</sup>
elective				
emergent	18.8	7.4 <sup>a</sup>	8.2 <sup>a</sup>	19.4 <sup>b</sup>
nonsurgical	8.7	8.9 <sup>b,c</sup>	11.7 <sup>b</sup>	8.6 <sup>c</sup>
Organ failure (%)	72.5	83.7 <sup>a</sup>	80.1 <sup>a</sup>	71.9 <sup>b</sup>
0				
1	43.3	43.1 <sup>a</sup>	16.4 <sup>b</sup>	44.3 <sup>a</sup>
2	41.6	38.1 <sup>b,c</sup>	37.3 <sup>b</sup>	41.8 <sup>c</sup>
≥3	11.8	13.1 <sup>a</sup>	32.1 <sup>b</sup>	11.1 <sup>a</sup>
elective	3.3	5.7 <sup>a</sup>	14.2 <sup>b</sup>	2.8 <sup>c</sup>
Temperature (°C)	36.8	36.7 <sup>a</sup>	36.7 <sup>a</sup>	36.8 <sup>a</sup>
MAP (mmHg)	79	77 <sup>a</sup>	67 <sup>b</sup>	79 <sup>a</sup>
Heart rate (/min)	85	87 <sup>a</sup>	106 <sup>b</sup>	84 <sup>a</sup>
Respiratory rate (/min)	20	22 <sup>a</sup>	25 <sup>b</sup>	20 <sup>c</sup>
PaO <sub>2</sub> (FiO <sub>2</sub> <0.5)	110	115 <sup>a</sup>	128 <sup>b</sup>	109 <sup>a</sup>
Serum sodium (mmol/L)	139.0	137.8 <sup>a</sup>	138.3 <sup>a,b</sup>	138.8 <sup>b</sup>
Serum potassium (mmol/L)	4.0	4.7 <sup>a</sup>	4.4 <sup>b</sup>	4.0 <sup>c</sup>
Serum creatinine (mmol/L)	122	577 <sup>a</sup>	359 <sup>b</sup>	103 <sup>c</sup>
Hematocrit (%)	33	29 <sup>a</sup>	28 <sup>a</sup>	33 <sup>b</sup>
WBC count (×10 <sup>3</sup> )	13	14 <sup>a</sup>	16 <sup>b</sup>	13 <sup>c</sup>
GCS Score	14	13 <sup>a</sup>	12 <sup>b</sup>	14 <sup>c</sup>
APACHE II	15	24 <sup>a</sup>	27 <sup>b</sup>	15 <sup>c</sup>
Renally adjusted APACHE II <sup>d</sup>	14	20 <sup>a</sup>	22 <sup>b</sup>	14 <sup>c</sup>
TISS score	23	23 <sup>a</sup>	37 <sup>b</sup>	23 <sup>a</sup>
Readmission ≤3 d (%)	2.2	4.6 <sup>a</sup>	4.6 <sup>a</sup>	2.4 <sup>b</sup>
Readmission during same hospitalization (%)	6.2	15.0 <sup>a</sup>	12.5 <sup>a</sup>	5.2 <sup>b</sup>
In-hospital mortality (%)	10.8	15.5 <sup>a</sup>	40.7 <sup>b</sup>	9.6 <sup>c</sup>

<sup>a,b,c</sup>Different superscripts denote statistically significant differences. ANOVA was used for normally distributed measures, Kruskal-Wallis test for non-Gaussian distributions,  $\chi^2$  test for dichotomous variables. All *P* values were adjusted for three-way comparisons.

<sup>d</sup>See text. Calculated by subtracting renal component from APACHE II score

patients with ESRD remain undefined: We cannot know which or how many patients with ESRD were declined for admission to ICU and whether the criteria for admission differed systematically from those applied to nondialysis patients. It is possible that only “good” dialysis patients were selected for admission and thus that outcomes observed in the study are not reflective of all dialysis patients who are potential ICU candidates. In this regard, Hutchison *et al.*<sup>3</sup> noted that median age of admission to ICU of patients with ESRD was less than the median age of prevalent patients with ESRD in the United Kingdom and concluded that referral filter biases against older dialysis patients probably existed. This was not observed in our study. Moreover, patients with ESRD had greater comorbidity and higher

illness severity scores, arguing against strong admission filter biases on the basis of perceived illness severity. The study analyzed data from an existing clinical database of ICU patients. Clinical databases may suffer from incompleteness and inaccuracy of data, and, in some cases, data are entered retrospectively; however, the database used for this study was comprehensive and prospective, with mandatory data entry by dedicated program research nurses as part of the admission process, likely mitigating some of these weaknesses. We used a more liberal definition of long-term dialysis in our study (6 wk on dialysis *versus* 12 wk) than has been used in large registry studies. This may have biased our ESRD group toward inclusion of sicker patients and higher mortality; however, the di-

**Table 3.** Logistic regression model describing impact of ESRD status on in-hospital mortality with forced adjustment for case mix and physiologic variables

Variable	OR	95% CI	P
ESRD	0.90	0.68 to 1.19	0.5
Age (yr)			<0.0001
<45.0	Reference		
45.0 to 54.9	1.26	1.03 to 1.55	
55.0 to 64.9	1.709	1.415 to 2.063	
65.0 to 74.9	2.166	1.807 to 2.595	
≥75.0	3.070	2.575 to 3.659	
Male gender	0.94	0.85 to 1.04	0.2
Diabetes	0.92	0.82 to 1.03	0.2
Ischemic heart disease	0.99	0.86 to 1.14	0.9
Stroke	1.04	0.88 to 1.23	0.6
Peripheral arterial disease	1.08	0.94 to 1.25	0.3
Arrest	1.42	1.22 to 1.65	<0.0001
Sepsis	1.37	1.19 to 1.58	<0.0001
Mechanical ventilation	1.83	1.62 to 2.08	<0.0001
Cancer	1.20	1.06 to 1.37	0.006
Surgical status			<0.0001
nonsurgical	Reference		
elective surgery	0.31	0.25 to 0.38	
emergent surgery	0.68	0.58 to 0.80	
Organ system failure (n)			<0.0001
0	Reference		
1	2.28	1.98 to 2.63	
2	4.04	3.41 to 4.77	
≥3	6.69	5.23 to 8.55	
Temperature (°C)			0.0002
<36.0	1.51	1.35 to 1.69	
36.0 to 38.5	Reference		
>38.5	0.98	0.86 to 1.12	
Mean arterial pressure (mmHg)			<0.0001
<70	1.94	1.69 to 2.24	
70 to 110	Reference		
>110	1.18	1.00 to 1.40	
Heart rate (/min)			<0.0001
<50	0.92	0.78 to 1.10	
50 to 100	Reference		
>100	1.72	1.54 to 1.92	
Respiratory rate (/min)			<0.00001
<14	0.78	0.68 to 0.89	
14 to 25	Reference		
>25	1.47	1.31 to 1.66	
PaO <sub>2</sub> (FiO <sub>2</sub> <0.5)			0.3
≥60	Reference		
<60	1.06	0.96 to 1.18	
Serum sodium (mmol/L)			<0.00001
<130	1.49	1.23 to 1.82	
130 to 150	Reference		
>150	1.51	1.23 to 1.85	
Serum potassium (mmol/L)			0.001
<3.5	0.86	0.77 to 0.96	
3.5 to 5.5	Reference		
>5.5	1.32	1.11 to 1.56	
Serum creatinine (mmol/L)			<0.00001
≤133	Reference		
>133	1.69	1.54 to 1.86	

**Table 3.** (Continued)

Variable	OR	95% CI	P
Hematocrit (%)			0.8
<30	1.02	0.92 to 1.14	
WBC count (×10 <sup>3</sup> /mm <sup>3</sup> )			<0.00001
<3	2.78	2.21 to 3.50	
3 to 15	Reference		
>15	1.32	1.19 to 1.46	
GCS score			<0.00001
<7	Reference		
7 to 12	0.31	0.26 to 0.36	
>12	0.17	0.15 to 0.20	

Model  $P < 0.00001$ ; area under the receiver operating characteristic curve 0.89. CI, confidence interval; FiO<sub>2</sub>, fraction of inspired oxygen.

rection of this bias (*i.e.*, overestimate of true mortality associated with ESRD status) is unlikely to alter the conclusion that ESRD status was not associated with mortality after adjustment. We used in-hospital mortality as our primary outcome measure. This statistic probably underestimates true mortality, because some patients may have died after hospital discharge. Finally, our results describe observations in a single region, and thus generalizability across other regions of the United States and Canada has not been directly established. Nevertheless, the consistency of our findings regarding the adjusted risk for mortality attributable to ESRD status across regions (Europe, United States, and Canada) is reassuring.

In conclusion, patients with ESRD were admitted to the ICU much more frequently than that observed for the general population. Although patients with ESRD did fare worse than patients without ESRD, their mortality was half that observed for patients with AKI. Most of the adverse prognosis associated with ESRD status was attributable to comorbidities and illness severity, rather than ESRD status itself. Our findings are congruent with studies in other regions of the world and suggest that at most a modest increase in mortality is associated with ESRD in the ICU. We suggest that decisions about ICU admission and treatment for dialysis patients should be based on comorbidities and illness severity, not on ESRD status.

## CONCISE METHODS

### Study Population

The study population consisted of all adult patients who were admitted to any of the 11 ICUs serving the city of Winnipeg, Manitoba, Canada, during a 7-yr period from January 1, 2000, to December 31, 2006. Winnipeg is the tertiary care referral center for the entire province of Manitoba (2006 population: 1,148,400). The ICUs included two primarily surgical and nine primarily medical ICUs. Significant overlap in the type of patient treated in surgical *versus* medical ICU frequently occurred, because patients were often transferred between designated surgical and medical ICUs in accordance with bed availability, irrespective of diagnosis. Seven of the ICUs were in tertiary care teaching hospitals, whereas four ICUs were in



**Table 4.** Reduced logistic regression model of major predictors of in-hospital mortality

Variable	OR	95% CI	P
Age (yr)			<0.0001
<45.0	Reference		
45.0 to 54.9	1.26	1.03 to 1.54	
55.0 to 64.9	1.700	1.410 to 2.064	
65.0 to 74.9	2.170	1.820 to 2.593	
≥75.0	3.13	2.64 to 3.71	
Arrest	1.41	1.21 to 1.64	<0.0001
Sepsis	1.38	1.20 to 1.59	<0.0001
Mechanical ventilation	1.80	1.60 to 2.03	<0.0001
Cancer	1.20	1.06 to 1.37	0.005
Surgical status			<0.0001
nonsurgical	Reference		
elective surgery	0.31	0.26 to 0.38	
emergent surgery	0.69	0.59 to 0.81	
Organ system failure (n)			<0.0001
0	Reference		
1	2.28	1.98 to 2.63	
2	4.04	3.42 to 4.78	
3 or more	6.73	5.28 to 8.60	
Temperature (°C)			0.0002
<36.0	1.51	1.35 to 1.69	
36.0 to 38.5	Reference		
>38.5	0.98	0.86 to 1.12	
Mean arterial pressure (mmHg)			<0.0001
<70	1.95	1.70 to 2.25	
70 to 110	Reference		
>110	1.18	0.99 to 1.39	
Heart rate (/min)			<0.0001
<50	0.93	0.78 to 1.10	
50 to 100	Reference		
>100	1.72	1.54 to 1.92	
Respiratory rate (/min)			<0.00001
<14	0.78	0.68 to 0.89	
14 to 25	Reference		
>25	1.47	1.31 to 1.66	
Serum sodium (mmol/L)			<0.00001
<130	1.49	1.23 to 1.82	
130 to 150	Reference		
>150	1.51	1.23 to 1.85	
Serum potassium (mmol/L)			0.002
<3.5	0.87	0.78 to 0.97	
3.5 to 5.5	Reference		
>5.5	1.30	1.10 to 1.54	
Serum creatinine (mmol/L)			<0.00001
≤133	Reference		
>133	1.69	1.54 to 1.86	
WBC count ( $\times 10^3/\text{mm}^3$ )			<0.00001
<3	2.80	2.23 to 3.51	
3 to 15	Reference		
>15	1.32	1.19 to 1.46	
GCS score			<0.00001
<7	Reference		
7 to 12	0.31	0.26 to 0.37	
>12	0.17	0.15 to 0.20	

Model  $P < 0.00001$ ; area under the receiver operating characteristic curve 0.89.

community hospitals. The ICUs at the two teaching hospitals were dialysis capable, whereas the community ICUs were not. All patients who required dialysis (long- or short-term) were transferred as soon as possible to one of the dialysis-capable ICUs. High-acuity patients without renal failure were also routinely transferred to the tertiary care teaching hospitals to access services not available in the community. All ICUs were closed units managed by an attending intensivist and a dedicated ICU staff. All renal replacement therapy (intermittent hemodialysis or continuous venovenous hemodiafiltration) was managed by nephrologists.

### Data Collection

The electronic database for the ICUs is a regional, prospectively maintained database of all patients who are admitted to any of the 11 ICUs in Winnipeg. Data collection for the database is a mandatory part of the admission process. Clinical admission and discharge diagnoses are entered in real time by the attending intensivist. All other clinical data are entered by one of several full-time research nurses employed by the regional ICU program. The database tracks patients from ICU admission to death or hospital discharge. All data sheets are audited for completeness by research nurses at the time of discharge from ICU and at hospital discharge. When necessary, a chart review to identify missing data elements is performed. Collected data include patient demographics, admitting and discharge diagnoses (primary and up to five secondary diagnoses for each), illness severity indicators including all elements of the APACHE II and euroSCORE (European System for Cardiac Operative Risk Evaluation) on admission, admission serum creatinine, daily TISS scores to quantify type and number of ICU interventions, disposition, and in-hospital survival.

### Cohort Definitions

ESRD status on admission was prospectively collected and defined in the database as ongoing need for peritoneal dialysis or ongoing need for hemodialysis beyond 6 wk after initiation. AKI was defined as acute or acute on chronic renal dysfunction severe enough to require renal replacement therapy of any form (*e.g.*, continuous venovenous hemodiafiltration) at any point during the ICU admission. The need for acute dialysis was coded directly, prospectively, and unambiguously in the database. Because the ICU database included only the admission creatinine value, it was not possible to define less severe forms of AKI using percentage or absolute serum creatinine rise.

### Outcome Definitions

The primary outcome was in-hospital mortality. The ICU database tracks all patients from ICU admission to final discharge from hospital or death, so in-hospital mortality and LOS were known for all patients. The TISS,<sup>10</sup> which quantifies type and number of ICU interventions and is an accepted measure of ICU resource use and workload, was calculated and entered daily into the ICU database.

## Data Analysis

Continuous variables of interest were summarized as mean (SD). Dichotomous variables and outcomes were summarized as percentages. *T* tests and ANOVA were used to compare normally distributed measures. The Mann-Whitney *U* test and the Kruskal-Wallis test were used for non-Gaussian distributions. The  $\chi^2$  test was used to compare dichotomous variables.

Crude yearly ICU admission rates for patients with ESRD were calculated as the number of ESRD admissions divided by the number of prevalent patients registered in the Manitoba Renal Program registry at the end of that year. Because patients with ESRD are older and have a greater proportion of men, we adjusted the crude rates by age and gender by direct standardization against the 2006 adult population of Manitoba. Admission rates for patients without ESRD were calculated as the number of non-ESRD ICU admissions divided by the adult population of Manitoba in 2006.

We used multiple logistic regression to adjust the OR for death associated with ESRD status for baseline case-mix and physiologic variables. To avoid potential distortions as a result of the nonindependence of repeated admissions, we restricted the analysis to first admissions. Because our main objective was comprehensive adjustment, variables were included in the first model (Table 3) on the basis of either statistical significance or potential biologic importance. A second, reduced model was also derived using backward stepping (Table 4). Because death and readmission to ICU are competing and mutually exclusive outcomes, analysis of first admissions could underestimate mortality in groups with higher readmission rate. For this reason, we performed a sensitivity analysis using last admissions. All analyses were performed using SAS 9.1.3.

## DISCLOSURES

None.

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